

## **REMARKS**

### **Status of the Claims**

#### *Pending claims*

Claims 8 to 77 are pending (claims 1 to 7 as filed were canceled).

#### *Restriction Requirement and Election*

In the restriction requirement dated December 26, 2001, the Patent Office alleged that the pending claims of the application were directed to three separate and distinct inventions under 35 U.S.C. §121:

Group I: Claims 8-41 and 63-64, drawn to a modified biological molecule, a microarray, classified in class 530, subclass 300, class 536 and subclass 123.1, class 436 and subclass 71, and 518.

Group II: Claims 42-62, drawn to a method for immobilizing a biological molecule, classified in class 435, subclass 6.

Group III: Claim 65, drawn to a kit comprising a device for imprinting an array, classified in class 436, subclass 518.

In response to the Restriction Requirement, Applicants elected Group I, claims 8 to 41 and 63 to 64, drawn to a modified biological molecule, a microarray, classified in class 530, subclass 300, class 536 and subclass 123.1, class 436 and subclass 71, and 518.

New claims 66 to 77, added in Applicants' response of October 29, 2001, to the (second) Restriction Requirement, mailed September 28, 2001, have been withdrawn from consideration for reading on a non-elected invention.

#### *Claims amended and added in the instant amendment*

Claims 8 to 17, 25 to 33, 35, 39, 41, 63 and 64 are amended and new claims 78 to 86 are added. Thus, after entry of the instant amendment, claims 8 to 86 will be pending, and, claims 8 to 41, 63 to 64 and 78 to 86 will be pending and under consideration.

#### *Withdrawn Rejections*

Applicants thank the Examiner for noting that the rejections made under 35 U.S.C. §112, second paragraph and 35 USC §102(b) in the previous office action have been withdrawn.

Applicant : Bradley et al.  
Serial No. : 09/546,085  
Filed : April 10, 2000  
Page : 10

Attorney's Docket No.: 11635-010001 / OTA 97-63

### *Outstanding Rejections*

Claims 8, 13 to 17, 22 to 25, 27, 31 to 34, 37 and 39 to 41 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1 to 4, 7 to 10, 18 to 20, 25 to 28 and 33 to 34 of U.S. Patent No. 6,048,695. Claims 8 to 25 and 27 to 32 are rejected under 35 U.S.C. §101 as allegedly claiming the same invention as that of claims 1 to 4, 8 to 11, 18, 20 to 28 and 54 of co-pending USSN 09/853,343. Claims 8 to 24, 35 to 38 and 63 to 64 stand rejected under 35 U.S.C. §112, second paragraph. Claims 8, 9, 12 to 18, 21, 23, 24, 63 and 64 are rejected under 35 USC 102(b) as allegedly anticipated by Krinski et al. U.S. Patent No. 4,713,116 (hereinafter "Krinski"). Claims 25 and 27 to 30 are rejected under 35 USC 102(b) as allegedly anticipated by Plueddemann, U.S. Patent No. 4,231,910 (hereinafter "Plueddemann"). Claims 25 to 29 and 31 to 32 are rejected under 35 USC 102(e) as allegedly anticipated by Beattie, U.S. Patent No. 6,426,183, filed August 14, 1998, which is a CIP of an application filed December 19, 1996 (now U.S. Patent No. 6,156,502, with a provisional priority document filed December 21, 1995) (hereinafter "Beattie").

Applicants respectfully traverse all outstanding objections to the specification and rejections of the claims.

### Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to compositions and methods for making and using modified biological molecules, including nucleic acids, such as DNA and RNA, polypeptides or peptides, such as antibodies, polysaccharides, lipids, and small molecules, can be found, *inter alia*, on page 8, lines 9 to 16; page 14, lines 11 to 20; and Examples 18 and 19, page 19, line 14 to page 21, line 2.

### Double Patenting Issues

#### *Obviousness-type double patenting*

Claims 8, 13 to 17, 22 to 25, 27, 31 to 34, 37 and 39 to 41 are rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1 to 4, 7 to 10, 18 to 20, 25 to 28 and 33 to 34 of U.S. Patent No. 6,048,695. The instant

application is a CIP of U.S. Patent No. (USPN) 6,048,695. Applicants will hold this issue in abeyance until such time claims are held allowable.

*Statutory-type double patenting*

Claims 8 to 25 and 27 to 32 (claims 8 and 17 are independent claims, the remainder are dependent) are rejected under 35 U.S.C. §101 as allegedly claiming the same invention as that of claims 1 to 4, 8 to 11, 18, 20 to 28 and 54 of co-pending USSN 09/853,343 (claims 1 and 23 are independent claims, the remainder are dependent). USSN 09/853,343 is a CIP of the instant application, which is a CIP of USPN 6,048,695.

*Co-pending USSN 09/853,343*

Claim 1 of co-pending USSN 09/853,343 reads:

1. A modified biological molecule comprising a biological molecule modified by reaction with a compound having the formula:  $R_1 - X - R_2$ , wherein  $R_1$  is a cyclic ether group or an amino group,  $R_2$  is an alkoxy silane group and  $X$  comprises a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxy silane group.

Claim 23 of co-pending USSN 09/853,343 reads:

23. An article of manufacture comprising an arrayed plurality of biological molecules covalently bound to a surface,

wherein, before attachment to the surface, the biological molecules are modified by reaction with a compound having the formula:  $R_1 - X - R_2$ , wherein  $R_1$  is a cyclic ether group or an amino group,  $R_2$  is an alkoxy silane group and  $X$  is a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxy silane group, and upon attachment to the surface the modified biological molecules are covalently bound to the surface;

wherein each biological molecule is attached to the surface on at least one discrete and known location to form a cluster of substantially identical biological molecules.

*The instant application*

Pending claim 8 of the instant application reads:

8. A modified biological molecule comprising a biological molecule covalently bound to a compound having the formula:  $R_1 - X - R_2$ , wherein  $R_1$  is a cyclic ether group,  $R_2$  is an alkoxy silane group; and  $X$  is a moiety chemically suitable for linking the cyclic ether group and the alkoxy silane group.

Pending claim 8 after entry of the instant amendment reads:

8. (Amended) A composition comprising a nucleic acid, a polysaccharide or a saccharide, a lipid, an antibody or a small molecule covalently bound to a compound

having the formula:  $R_1 - X - R_2$ , wherein  $R_1$  is a cyclic ether group,  $R_2$  is an alkoxy silane group; and  $X$  is a moiety chemically suitable for linking the cyclic ether group and the alkoxy silane group.

Pending claim 17 of the instant amendment reads:

17. A modified biological molecule comprising a biological molecule covalently bound to a compound having the formula:  $R_1 - X - R_2$ , wherein  $R_1$  comprises an amino group,  $R_2$  comprises an alkoxy silane group; and  $X$  comprises a moiety chemically suitable for linking the amino group and the alkoxy silane group.

Pending claim 17 after entry of the instant amendment reads:

17. (Amended) A modified biological molecule covalently bound to a compound having the formula:  $R_1 - X - R_2$ , wherein  $R_1$  comprises an amino group,  $R_2$  comprises an alkoxy silane group; and  $X$  comprises a moiety chemically suitable for linking the amino group and the alkoxy silane group.

Applicants respectfully aver that claims 1 and 23 of co-pending USSN 09/853,343 clearly differ in scope from that of pending or amended claim 8 and 17 of the instant application. Accordingly, the statutory-type double patenting rejection under 35 U.S.C. §101 can be properly withdrawn.

#### Issues under 35 U.S.C. §112, second paragraph

Claims 8 to 24, 35 to 38 and 63 to 64 stand rejected under 35 U.S.C. §112, second paragraph.

##### *The phrase "a moiety chemically suitable"*

The Patent Office alleges the phrase "a moiety chemically suitable" is indefinite or unclear. The instant amendment addresses this issue.

##### *Product or process*

The Patent Office alleges that the claims 33 to 38 are indefinite because it is not clear whether the claims are drawn to a product or process. The instant amendment addresses this issue.

#### Issues under 35 U.S.C. §102(b)

##### *Krinski et al. U.S. Patent No. 4,713,116*

Claims 8, 9, 12 to 18, 21, 23, 24, 63 and 64 are rejected under 35 USC 102(b) as allegedly anticipated by Krinski et al. U.S. Patent No. 4,713,116.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

The Patent Office alleges, inter alia, that Krinski teaches a modified biological molecule (protein) covalently bound to a compound having a formula  $R_1 - X - R_2$  and the compound could be glycoxypropyltrimethoxysilane. The Patent Office also alleges that the modified biological molecule could be a protein material, a peptide or a polypeptide and that the alkoxysilane could be a propyl trimethyl silane.

Krinski only teaches modifying protein materials with organosilanes such as the alkoxysilane 3-glycidoxypolypropyltrimethoxysilane (see, e.g., column 4, lines 31 or 41, of Krinski). Krinski is clearly focused on modifying vegetable protein materials, see, e.g., column 3, line 6 to column 4, line 30, of Krinski. For example, the Summary, column 2, lines 37 to 49, read:

These and other objects are achieved in the present invention by the production of a modified vegetable protein adhesive binder having good rheological and paper coating characteristics. The present invention provides a process for the production of a modified vegetable protein adhesive binder which is suitable for use in pigment coating compositions wherein the process of producing the modified binder comprises forming an alkaline dispersion of a vegetable protein material followed by reaction of the dispersion with an organosilane reagent in an amount sufficient to modify the protein material.

Krinski only discusses modifying vegetable protein materials. Krinski does not teach or suggest modifying protein materials with any molecule other than with organosilanes, such as alkoxysilanes.

The Patent Office alleges that Krinski could include addition of amino groups to the modified biological molecule, citing column 4, lines 54 to 67. Applicants respectfully aver that Krinski does not teach or suggest addition of amino groups to a modified protein. The paragraph encompassing column 4, lines 54 to 67 reads in full:

Although the present invention has not intended to be limited by the exact types of coating compositions in which the modified protein adhesive binder of the present invention may be employed; nevertheless, typical coating compositions which employ the modified protein adhesive binder of the present invention generally include ingredients such as pigments, fluidizers or thinning agents, as well as various other ingredients such as optical brighteners and co-binders such as acrylic or styrene-butadiene latexes. Typically the modified vegetable protein adhesive binder of the present

invention is dispersed in a solubilizing agent such as an alkaline material, typically sodium carbonate, ammonium hydroxide, sodium hydroxide and the like. These materials provide a conventional means of solubilizing various types of protein materials for use as adhesive binders in paper coating compositions. The exact amount of protein isolate used to prepare the binder solution is at a level sufficient to form an adhesive binder, for the pigment coating and typically of a sufficient level so when the coating composition with the mineral pigment is prepared about 1 to 20% by weight of the coating comprises binder.

In fact, Krinski teaches away from adding amino groups to (vegetable) protein material, noting that it is the various primary amino groups of the vegetable protein materials that can be modified, as discussed, *inter alia*, on column 2, lines 50 to 57:

Preferably, the organosilane reagent is a silanation reagent such as an alkoxy silane reagent, most preferably an alkene alkoxy silane reagent, such as an alkene trialkoxy silane reagent. Modification of the protein material with the acrylate reactant occurs through modification of the various primary amino groups which are present in the amino acid residues of the vegetable protein material. [emphasis added]

In considering the instant response and amendment, Applicants respectfully aver that Krinski is not a single prior source that contains each and every limitation of claims 8, 9, 12 to 18, 21, 23, 24, 63 and 64. Accordingly, this rejection under section 102(b) can be properly withdrawn.

*Plueddemann, U.S. Patent No. 4,231,910*

Claims 25 and 27 to 30 are rejected under 35 USC 102(b) as allegedly anticipated by Plueddemann, U.S. Patent No. 4,231,910.

The Patent Office alleges that Plueddemann, entitled "Primer composition," teaches a modified biological molecule (primer compositions) on a solid support, citing column 2, lines 21 to 39 (see office action mailed 8/28/02 of co-pending 09/853,343) and column 3, lines 22 to 29.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

Applicants respectfully aver that Plueddemann does not teach or suggest modifying any biological molecule. In fact, the primer composition of Plueddemann is a primer

composition for application to a solid substrate to provide improved adhesion with thermoplastics, not an oligonucleotide "primer."

Plueddemann does not teach or suggest modifying any biological molecule, for example, in column 2, lines 21 to 39, these lines read:

In accordance with the present invention the primer composition contains an organosilicon compound. The organosilicon compound can be 3-glycidoxypolytrimethoxysilane, 2-(3,4-epoxycyclohexyl)-ethyltrimethoxysilane, 2-mercaptopropyltrimethoxysilane or 3-mercaptopropyltrimethoxysilane which are well known and commercially available compounds. In addition partial hydrolyzates of these silanes can be utilized in the primer compositions. "Partial hydrolyzate" is meant to imply that the silane has been hydrolyzed with water, but that a detectable amount of hydroxyl or methoxy groups remain uncondensed in the composition. It is preferable that one such group per every four silicon atoms remain uncondensed.

When the primer composition is to be stored some time before use, it is preferred to employ 3-glycidoxypolytrimethoxysilane in the primer composition for improved stability.

See also, e.g., column 3, lines 22 to 29, which also do not teach or suggest modifying any biological molecule; these lines read:

The primer compositions are utilized to increase both wet and dry adhesion of thermoplastics to solid substrates. The solid substrate can be any solid including siliceous material such as glass, quartz, ceramic, asbestos, silicone resin and glass fibers, metals such as aluminum, steel, copper, nickel, magnesium, and titanium, metal oxides such as MgO, Fe<sub>2</sub>O<sub>3</sub>, and Al<sub>2</sub>O<sub>3</sub>, or an organic solid such as wood, rubber or plastic materials.

As noted above, the primer composition of Plueddemann is a primer composition to provide improved adhesion with thermoplastics. It is not an oligonucleotide "primer." For example, as stated in the Summary (see column 2, lines 3 to 18);

The present invention relates to a primer composition for application to a solid substrate to provide improved adhesion with thermoplastics, the composition consisting essentially of (A) 1 to 25 weight percent of an organosilicon compound selected from a group consisting of (1) 3-glycidoxypolytrimethoxysilane, (2) 3-mercaptopropyltrimethoxysilane, (3) 2-mercaptopropyltrimethoxysilane, (4) 2-(3,4-epoxycyclohexyl)-ethyltrimethoxysilane, and (5) partial hydrolyzates of (1), (2), (3) or (4) and (B) 75 to 99 weight percent of an alkoxymethyltriazine which is a product of etherification of a methyloltriazine with a monohydric alcohol having 4 carbons or less.

See also column 3, lines 1 to 9 and 61 to 64 of Plueddemann:

The primer compositions of the present invention contain 75 to 99 percent by weight alkoxyethyltriazine. When commercially available alkoxyethyltriazines which are supplied in solvents such as isopropanol, butanol and xylene are employed, sufficient solution is employed so that the weight of alkoxyethyltriazine is 75 to 99 percent of the combined weight of organosilicon compound and alkoxyethyltriazine excluding solvent weight.

The primer compositions of this invention are generally specific for the types of thermoplastics described above and do not work well with thermoplastics such as polystyrene, polyolefins and polyacetals.

Accordingly, Plueddemann is not a single prior source that contains each and every limitation of claims 25 and 27 to 30. Accordingly, this rejection under section 102(b) can be properly withdrawn.

*Beattie, U.S. Patent No. 6,426,183*

Claims 25 to 29 and 31 to 32 are rejected under 35 USC 102(e) as allegedly anticipated by Beattie, U.S. Patent No. 6,426,183, filed August 14, 1998.

The Patent Office cites Beattie for allegedly teaching microarrays comprising modified biological molecules and disclosing solid supports comprising silane-containing substrates which include hydroxyl groups, citing, *inter alia*, column 4, lines 46 to 54.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention.

Applicants respectfully aver that Beattie does not teach or suggest modification of any biological molecule covalently bound to a compound having the formula:  $R_1 — X — R_2$ , wherein  $R_1$  is a cyclic ether group,  $R_2$  is an alkoxy silane group; and  $X$  is a moiety chemically suitable for linking the cyclic ether group and the alkoxy silane group. Applicants respectfully aver that Beattie does not teach or suggest modification of any biological molecule covalently bound to a compound having the formula:  $R_1 — X — R_2$ , wherein  $R_1$  comprises an amino group,  $R_2$  comprises an alkoxy silane group; and  $X$  comprises a moiety chemically suitable for linking the amino group and the alkoxy silane group.

Beattie does not discuss modification of any biological molecule by reaction with a compound having silane. The silanes discussed in Beattie are in the substrate to which a

biological molecule is attached, not in the biological molecule to be attached to the substrate.

For example, the paragraph of column 4, lines 46 to 54 of Beattie, cited by the Patent Office, and the paragraph immediately preceding it read:

Silaceous Substrate or Silane-Containing Substrate or Material--In the present invention, this refers to a silaceous or silane-containing substrate or material, at least one surface of which comprises or has been treated to expose silanol groups. Examples thereof include the glasses identified above, porous silica materials, micromachined silicon, oxidized silicon materials, and materials coated with any of the foregoing.

Silane--Refers to  $S_{in}H_{2n+2}$ . Silane-containing compounds or substrates are generally gaseous or liquid compounds of silicon and hydrogen, analogs to alkanes or hydrocarbons.  $SiH_3$  is called silyl (analogous to methyl) and  $Si_2H_5$  is disilanyl (analogous to ethyl). A cyclic silicon and hydrogen compound having the formula  $SiH_2$  is called a cyclosilane. Organo-functional silanes are noted for their ability to bind organic polymers to inorganic substrates.

The silanes discussed in Beattie are in the substrate to which a biological molecule is attached, not in the biological molecule to be attached to the substrate. For example, see also column 1, lines 49 to 57, of Beattie, which reads:

The present invention provides a method for attaching a compound having at least one amine group and at least one hydroxyl group, to a silane-containing substrate, e.g., a glass, porous silica, oxidized silicon, or other silaceous or silane-containing material. More specifically, the present invention provides a method for attaching an aminopropanol-containing compound to a silane-containing substrate, e.g., a glass, porous silica, oxidized silicon, or a silanized material.

Accordingly, because Beattie does not teach or suggest any biological molecule covalently bound to a compound having the formula:  $R_1 — X — R_2$ , wherein  $R_1$  is a cyclic ether group,  $R_2$  is an alkoxy silane group; and  $X$  is a moiety chemically suitable for linking the cyclic ether group and the alkoxy silane group, or any biological molecule covalently bound to a compound having the formula:  $R_1 — X — R_2$ , wherein  $R_1$  comprises an amino group,  $R_2$  comprises an alkoxy silane group; and  $X$  comprises a moiety chemically suitable for linking the amino group and the alkoxy silane group, Beattie is not a single prior source that contains each and every limitation of claims 25 to 29 and 31 to 32, and this rejection under section 102(b) can be properly withdrawn.

Applicant : Bradley et al.  
Serial No. : 09/546,085  
Filed : April 10, 2000  
Page : 18

Attorney's Docket No.: 11635-010001 / OTA 97-63

Applicants also note that the priority document of the instant application (the instant application is a CIP of co-pending USSN 09/546,085, which is a CIP of U.S. Patent No. 6,048,695) is a "reference cited" in Beattie.

### CONCLUSION

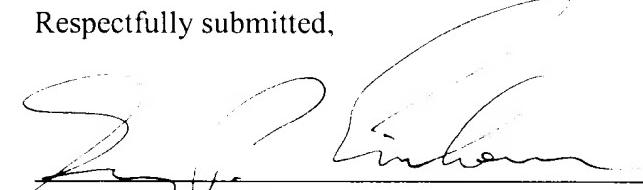
In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §101, 35 U.S.C. §112, second paragraph, and 35 U.S.C. §102(b). Applicants believe after entry of the instant amendment all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If necessary, please apply additional and necessary charges, and apply all credits, to Deposit Account No. 06-1050.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date: Feb. 19, 2003



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**Version with markings to show changes made**

**In the claims:**

The following claims have been amended as follows:

8. (Amended) A composition [modified biological molecule] comprising a [biological molecule] nucleic acid, a polysaccharide or a saccharide, a lipid, an antibody or a small molecule covalently bound to a compound having the formula:  $R_1 - X - R_2$ , wherein  $R_1$  is a cyclic ether group,  $R_2$  is an alkoxysilane group; and  $X$  is a moiety [chemically suitable for] linking the cyclic ether group and the alkoxysilane group.

9. (Amended) The composition [modified biological molecule] of claim 8, wherein the biological molecule comprises a nucleic acid [polypeptide or a peptide].

10. (Amended) The composition [modified biological molecule] of claim 8, wherein the biological molecule comprises a polysaccharide or a saccharide.

11. (Amended) The composition [modified biological molecule] of claim 8, wherein the biological molecule comprises a lipid.

12. (Amended) The composition [modified biological molecule] of claim 8, wherein the biological molecule comprises a small molecule.

13. (Amended) The composition [modified biological molecule] of claim 8, wherein the cyclic ether group comprises an epoxide group.

14. (Amended) The composition [modified biological molecule] of claim 13, wherein the epoxide group comprises an ethylene oxide.

15. (Amended) The composition [modified biological molecule acid] of claim 8, wherein the alkoxy silane is selected from the group consisting of —Si(OCH<sub>3</sub>)<sub>3</sub>, —Si(OC<sub>2</sub>H<sub>5</sub>)<sub>3</sub>, —Si(OCH<sub>3</sub>)H<sub>2</sub>, —Si(OCH<sub>3</sub>)(CH<sub>3</sub>)<sub>2</sub>, and —Si(OCH<sub>3</sub>)<sub>2</sub>CH<sub>3</sub>.

16. (Amended) The composition [modified biological molecule] of claim 8, wherein the compound is 3-glycidoxypropyltrimethoxysilane.

17. (Amended) A modified biological molecule [comprising a biological molecule] covalently bound to a compound having the formula: R<sub>1</sub> — X — R<sub>2</sub>, wherein R<sub>1</sub> [is] comprises an amino group, R<sub>2</sub> [is] comprises an alkoxy silane group; and X [is] comprises a moiety [chemically suitable for] linking the amino group and the alkoxy silane group.

25. (Amended) A microarray comprising:  
a solid support, and  
modified biological molecules covalently bound to a compound having the formula: R<sub>1</sub> — X — R<sub>2</sub>, wherein R<sub>1</sub> comprises an amino group, R<sub>2</sub> comprises an alkoxy silane group; and X comprises a moiety linking the amino group and the alkoxy silane group, [as set forth in claim 8 or claim 17], immobilized onto the solid support.

26. (Amended) The microarray of claim 25 or claim 82, wherein the solid support comprises hydroxyl groups.

27. (Amended) The microarray of claim 25 or claim 82, wherein the solid support comprises a glass.

28. (Amended) The microarray of claim 25 or claim 82, wherein the solid support comprises a surface selected from the group consisting of a quartz, a mica, an alumina, a titania, an SnO<sub>2</sub>, an RuO<sub>2</sub> and a PtO<sub>2</sub>.

29. (Amended) The microarray of claim 25 or claim 82, wherein the solid support comprises a metal oxide surface.

30. (Amended) The microarray of claim 25 or claim 82, wherein the solid support comprises a compound selected from the group consisting of a polystyrene, a polyester, a polycarbonate, a polyethylene, a polypropylene, and a nylon.

31. (Amended) The microarray of claim 25 or claim 82, wherein biological molecules are immobilized onto the solid support in orderly, discrete spots.

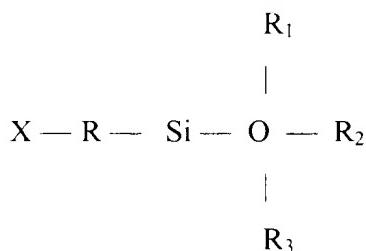
32. (Amended) The microarray of claim 31 or claim 82, wherein the discrete spots are about 50 microns in diameter.

33. (Amended) A modified biological molecule, wherein the biological molecule is prepared by a process comprising the steps of:

- (a) providing a biological molecule comprising a guanine base or a cytosine base;
- (b) reacting the guanine base or the cytosine base with an N-bromosuccinimide at pH about 8.0 to form a brominated biological molecule; and
- (c) reacting the brominated biological molecule with a silane having the formula —HN—(CH<sub>2</sub>)<sub>n</sub>—Si(OR)<sub>3</sub>, wherein n = 3, 4, 5, 6, 7, 8, or 9.

35. (Amended) A modified biological molecule, wherein the biological molecule is prepared by a process comprising the steps of:

- (a) providing a biological molecule;
- (b) providing a compound having a formula

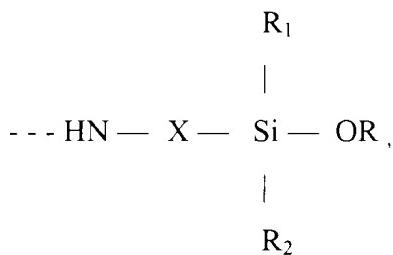


wherein X is a halide and R is a moiety [chemically suitable for] linking the biological molecule with the Si moiety;

(c) reacting the biological molecule with the compound of step (b) at near neutral pH.

39. (Amended) A modified biological molecule [comprising a biological molecule] covalently bound to a compound having the formula: —HN—(CH<sub>2</sub>)<sub>n</sub>—Si(OR)<sub>3</sub>, wherein n = 3, 4, 5, 6, 7, 8, or 9.

41. (Amended) A modified biological molecule [comprising a biological molecule] covalently bonded to a compound having the formula:



wherein R is selected from the group consisting of —CH<sub>3</sub>, —C<sub>2</sub>H<sub>5</sub>, and —C<sub>3</sub>H<sub>7</sub>, and R<sub>1</sub> and R<sub>2</sub> are the same or different and are selected from the group consisting of —H, —CH<sub>3</sub>, —C<sub>2</sub>H<sub>5</sub>, —OCH<sub>3</sub>, —OC<sub>2</sub>H<sub>5</sub>, —C<sub>3</sub>H<sub>7</sub>, and —OC<sub>3</sub>H<sub>7</sub>; and X is a linking group comprising an at least partially aliphatic chain.

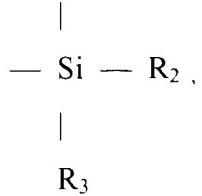
63. (Amended) A modified biological molecule comprising a biological molecule covalently bound to a compound having the formula: R<sub>1</sub> — X — R<sub>2</sub>; wherein R<sub>1</sub> [is] comprises a cyclic ether; wherein R<sub>2</sub> [is] comprises a —NR<sub>3</sub>, R<sub>3</sub> [is] comprises a —H or an alkyl group and X [is] comprises a moiety [chemically suitable for] linking the cyclic ether group and the alkoxy silane group.

64. (Amended) A modified biological molecule comprising a biological molecule covalently bonded to a compound having the formula



Applicant : Bradley et al.  
Serial No. : 09/546,085  
Filed : April 10, 2000  
Page : 23

Attorney's Docket No.: 11635-010001 / OTA 97-63



wherein R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are the same or different, and are selected from the group consisting of —OCH<sub>3</sub>, —OC<sub>2</sub>H<sub>5</sub>, —OC<sub>2</sub>H<sub>7</sub>, and —Cl, and X is a moiety[ , chemically suitable for] linking the biological molecule to the compound.

New claims 78 to 86 have been added.